

E1

USSN - 09/101,825

wherein at least one of the following conditions (I)-(V) is true:

I) at least one of  $X_A$ ,  $X_B$ ,  $X_C$ ,  $X_4$ ,  $X_5$  or  $X_6$  is a non-natural or unusual amino acid,

II) the polypeptide is cyclized,

III) the polypeptide is stabilized,

IV) the aminoterminal amino acid residue is acylated, or

V) the carboxyterminal amino acid residue is amidated,

where, if the polypeptide is not cyclized, said sequence corresponds essentially to the C-terminal of said polypeptide, said polypeptide having at least one of the following properties:

a) induces inhibition of spontaneous IL-8 production by human monocytes,

b) induces inhibition of IL-1 $\beta$  induced IL-8 production by human peripheral blood mononuclear cells (PBMC),

c) induces production of interleukin-1 receptor antagonistic protein (IRAP) by human monocytes,

d) induces chemotactic migration of CD8+ human T lymphocytes in vitro,

e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,

f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,

g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,

h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN- $\gamma$ ,

i) induces the production of IL-4 by cultured normal human CD4+ T cells,

j) reduces TNF $\alpha$  production in human mixed leukocyte reaction, or

k) downregulates TNF $\alpha$  and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

Concluded

E2

41 (amended). A pharmaceutical composition comprising a

polypeptide according to claim 18, or a salt, ester or solvate of said polypeptide.

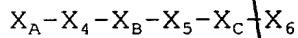
Please add the following new claims:

73 (new). The polypeptide of claim 18 where said amino acids each have a molecular weight not exceeding that of Fmoc-His(Trt)-OPfp (785.78 daltons).

74 (new). The polypeptide of claim 18 where said amino acids, other than  $X_A$ ,  $X_B$ ,  $X_C$ ,  $X_4$ ,  $X_5$  or  $X_6$ , are alpha or beta amino acids.

75 (new). The polypeptide of claim 18 which is not more than 15 a.a. in length.

76 (new). A non-naturally occurring polypeptide, or a polypeptide in at least partially purified form, which is six to 20 amino acids in length, and which comprises the following sequence



wherein  $X_4$  and  $X_5$  are independently selected from the group consisting of Met, Ile, Leu, Val, norvaline, norleucine, methionine-S-oxide, N-methylvaline, N-methyl isoleucine, allo-leucine, and their D-isomers;

$X_6$  is selected from the group consisting of Asn, Asp, Gln, Glu, and their D-isomers,

$X_A$  is L-Thr or a non-natural or unusual amino acid,

$X_B$  is L-Lys or a non-natural or unusual amino acid,

$X_C$  is L-Arg or a non-natural or unusual amino acid,

$X_4$  and  $X_5$  are independently selected from the group consisting of L-Met, L-Ile, L-Leu, L-Val and a non-natural or unusual amino acid,

$X_6$  is L-Asn, L-Asp, L-Gln, L-Glu, or a non-naturally or unusual amino acid,

no more than one of  $X_A$ ,  $X_B$ ,  $X_C$ ,  $X_4$ ,  $X_5$  and  $X_6$  is a non-natural or unusual amino acid other than the D-isomer of an L-amino acid recited as possible at that position,

wherein at least one of the following conditions (I)-(V) is true:

~~Ex~~ ~~73~~ I) at least one of  $X_A$ ,  $X_B$ ,  $X_C$ ,  $X_4$ ,  $X_5$  or  $X_6$  is a non-natural or unusual amino acid,

II) the polypeptide is cyclized,

III) the polypeptide is stabilized,

IV) the aminoterminal amino acid residue is acylated, or

V) the carboxyterminal amino acid residue is amidated,

where, if the polypeptide is not cyclized, said sequence corresponds essentially to the C-terminal of said polypeptide, said polypeptide having at least one of the following properties:

a) induces inhibition of spontaneous IL-8 production by human monocytes,

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d) induces chemotactic migration of CD8+ human T lymphocytes in vitro,

e) desensitizes human CD8+ T cells resulting in an unresponsiveness towards rhIL-10,

f) suppresses the chemotactic response of CD4+ T human lymphocytes towards IL-8,

g) suppresses the chemotactic response of human monocytes towards MCAF/MCP-1,

h) inhibits class II MHC molecule expression on human monocytes stimulated by IFN- $\gamma$ ,

i) induces the production of IL-4 by cultured normal human CD4+ T cells,

j) reduces TNF $\alpha$  production in human mixed leukocyte reaction, or

k) downregulates TNF $\alpha$  and IL-8 production in a rabbit model of bile acid induced acute pancreatitis and reduces neutrophil infiltration in the lungs of the treated rabbits.

77 (new). The polypeptide of claim 76 where no more than one of the amino acids of said polypeptide which lie outside said